

Amendments to the Claims

Amendments to the Claims are reflected in the following Listing of Claims, which replaces all prior versions and listings of the claims.

Listing of Claims

1. (Currently amended) A method for intermediate to large scale production in a semi-solid culture medium of stock compositions of bacteriophage having a titer of at least 10^{11} pfu/ml and a total yield of at least 10^{15} total pfu comprising:

(a) growing bacteriophage in a semi-solid culture medium comprising

(i) a pre-incubated mixture of at least one bacterial strain and at least one phage type ~~further comprising and~~

(ii) a hydrocolloid at a concentration below [0.5] 0.3%[;] wherein the semi-solid culture medium is supported by a solid phase;

(b) incubating the semi-solid culture medium to reach bacterial lysis, thereby obtaining a phage lysate; and

(c) extracting a crude bacteriophage extract from the semi-solid culture medium, using an extraction medium, wherein the crude bacteriophage extract is obtained by sequential serial extractions and wherein the titer of the crude bacteriophage extract is at least 10^{11} pfu/ml and the bacteriophage yield is at least in the order of magnitude of 10^{15} to 10^{16} total pfu.

2. (Original) The method according to claim 1, wherein the volume of the semi-solid culture medium is in the range of 1-20 liters.

3. (Currently amended) The method according to claim 1, wherein the total volume of the extraction medium is in the range of 20 to 100 fold the volume of the semi-solid culture medium.

4. (Canceled)

5. (Original) The method according to claim 1, wherein the semi-solid culture medium comprises a hydrocolloid at a concentration of 0.25%-0.30%.

6. (Original) The method according to claim 1, wherein the hydrocolloid is selected from the group consisting of agar, agarose, starch, pectin, carrageenan, alginate, gelatin, gellan, konjak mannan, xanthan and gum, and combinations thereof.

7. (Original) The method according to claim 6, wherein the hydrocolloid is agar.

8. (Previously presented) The method according to claim 1, wherein the pre-incubated mixture comprises bacteria and bacteriophage at a ratio of from about 10^8 to about 10^9 bacterial colony forming units to one bacteriophage plaque.

9. (Canceled)

10. (Canceled)

11. (Currently amended) The method according to claim ~~[[10]]~~ 1, wherein the semi-solid culture medium is layered on top of a first supportive solid phase bottom layer to form a second top layer.

12. (Currently amended) The method according to claim ~~[[10]]~~ 1, wherein the solid phase comprises a hydrocolloid at a concentration range of 1.0-2.0%.

13. (Original) The method according to claim 12 wherein the solid phase comprises agar at a concentration range of 1.0-2.0%.

14. (Currently amended) The method according to claim ~~[[10]]~~ 1, wherein the volume of the solid phase is from about two to about ten fold the total volume of the semi-solid culture medium that it is intended to support.

15. (Canceled)

16. (Original) The method according to claim 1 wherein the titer of the crude bacteriophage extract is in a range of 5×10^{11} to 10^{12} pfu/ml.

17. (Canceled)

18. (Original) The method according to claim 1 further comprising purifying the crude bacteriophage extract to obtain a bacteriophage stock composition by a method selected from the group consisting of fractionation by PEG, CsCl gradient centrifugation, filtration, ultra-filtration, and column chromatography.

19. (Original) The method according to claim 18 wherein the purified bacteriophage stock composition is lyophilized.

20-43. (Canceled)

44. (Previously presented) The method according to claim 11 wherein the solid phase comprises a hydrocolloid at a concentration range of 1.0-2.0%.

45. (Previously presented) The method according to claim 44 wherein the solid phase comprises agar at a concentration range of 1.0-2.0%.

46. (Previously presented) The method according to claim 11 wherein the volume of the solid phase is from about two to about ten fold the total volume of the semi-solid culture medium that it is intended to support.

47. (Previously presented) The method according to claim 12 wherein the volume of the solid phase is from about two to about ten fold the total volume of the semi-solid culture medium that it is intended to support.

48. (Previously presented) The method according to claim 13 wherein the volume of the solid phase is from about two to about ten fold the total volume of the semi-solid culture medium that it is intended to support.

49. (Previously presented) The method according to claim 44 wherein the volume of the solid phase is from about two to about ten fold the total volume of the semi-solid culture medium that it is intended to support.

50. (Canceled)

51. (Previously presented) The method according to claim 45, wherein the volume of the solid phase is from about two to about ten fold the total volume of the semi-solid culture medium that it is intended to support.

52. (Previously presented) The method according to claim 8, wherein the pre-incubated mixture further comprises a rich medium.

53. (New) The method according to claim 1, wherein the sequential serial extraction comprises the steps of:

- (a) collecting the semi-solid culture medium;
- (b) adding fresh medium to the semi-solid culture medium to obtain a slurry;
- (c) mixing the slurry intensively;
- (d) centrifuging the slurry to obtain a supernatant comprising a crude bacteriophage extract;
- (e) collecting the obtained crude bacteriophage extract; and
- (f) repeating the aforementioned steps until the phage titer in the crude bacteriophage extract is at or below 10^{10} pfu/ml; wherein a crude bacteriophage extract having a total phage count of at least from about 10^{15} to about 10^{16} is obtained from about one liter of semi solid composition.

54. (New) The method according to claim 1 wherein the extracting medium comprises a sugar that reduces or abolishes bacterial phage-neutralizing activity.

55. (New) The method according to claim 54 wherein the sugar is present in the extracting medium at a concentration in the range of 0.2-2.0 M.

56. (New) The method according to claim 54 wherein the sugar is selected from the group consisting of N-acetyl-D-glucosamine, 2-deoxy-D-glucose, D-glucosamine, D-fructose, D-galactose, lactose, D-mannose, D-xylose, maltose, L-rhamnose, cellobiose, and sucrose.

57. (New) The method according to claim 56 wherein the sugar is selected from the group consisting of D-glucosamine, D-mannose, and L-rhamnose.

58. (New) The method according to claim 1 wherein said incubating the semi-solid culture medium is carried out at a temperature of about 37°C for a period of about 12 hours to about 24 hours.

59. (New) The method according to claim 58 wherein said incubating the semi-solid culture medium is carried out at a temperature of about 37°C for a period of about 14 hours to about 18 hours.